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RADIUM

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

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VOL. VI. OCTOBER, 1915 No. 1

A STUDY IN THE INTERNAL THERAPEUTICS OF RADIUM*

By SAMUEL DELANO, M.D., Boston, Mass.

In connection with this summary of the first Boston application of radium emanation therapeutics, it ought to be borne in mind that nothing has been used alongside that could in anyway influence results; neither drugs, nor in general any of those physical adjuncts such as change of air, of scene, of regimen, or of habits, that are so often pointed to as the real efficient agents in treatment at spas.

One important particular distinguishes this series from previous ones, viz., the mode of exhibiting the radium (*sc.* radium emanation). Radium emanation may be introduced in several ways, viz., by injection, by inhalation, by bath, and in solution by drinking. But rarely, however, has it been given conjointly with its source, radium, because this yoking up has not until now been generally available.

Loewenthal in his "Grundriss" endorses this, however, as the most desirable method of exhibiting emanation, viz., a radium salt in solution, which, after sealing, has produced the emanation within its own precincts.

In such a case there is present, after a month, that amount of emanation which is in equilibrium with the radium salt (what may be called the maximum-equilibrium-constant) and there is also the radium salt as well. This last has an infinite capacity in emanation and must give off a further amount in its passage through the body.

One microgram of radium referred to (abbreviated 1 mcgm. = 1/1000 of a milligram) means a solution of enough of a radium salt to yield that equivalent of radium element. The amount of emanation in equilibrium with this one microgram of element is a microcurie, the measurement of which is 2,700 Mache units.

The cases are not in any sense selected. On the contrary, it seemed worth while to take them as they fell—failures, successes, slight or

*Medical Record, LXXXVIII, pp. 137-143, July 24, 1915.

complete. This, because of the novelty of the subject and the meager use as yet made of radium emanation in this country.

Moreover, even if some of the cases are very thin in clinical results, they at least show that radium can be taken without untoward effects. In this connection, too, it may be said that the earliest cases have been observed for a period of eighteen months.

Rheumatism and Gout.

Case I.—*General Debility with Gouty Tendency.*—F., æt. 54. Pain in back of head—great toe reddened and sensitive—some eczema about foot, of long duration. Took 2 mcgm. radium daily and 3 radium baths a week. After about a month much improvement with disappearance of local signs in foot. Radium markedly diuretic and laxative. After four months, repeated for tonic action only. Then again in eight months with a swollen finger joint. On the third treatment writes. "There is no doubt that for me radium is a good tonic."

Case II.—F., æt. 46. Pain in back of neck with creaky vertebræ and knees. Had persisted good while—other treatment ineffective. Two micrograms of radium, sometimes three daily—60 altogether. No creaking in knees—very much improved—markedly laxative effect. Three months later remains in unusually good health without symptoms.

Case III.—*Gout.*—M., æt. 46. Previous history of three attacks of gravel with two small stones—large patches of eczema—pruritus ani for a year. Intestinal putrefaction with very loose discharges—foul breath and tongue—neuritis in shoulder for a year. Radium at three different times—(60 micrograms over space of six weeks) in course of year—completely freed from pruritus and eczema; marked tonic action; better condition of bowels and sweet breath. Had radium by cataphoresis for shoulder; neuritis has disappeared.

Case IV.—*Chronic Rheumatism Four Years.*—M., æt. 24. Motorman; pain in back, toes and wrists; interfered with work; much treatment including Mt. Clemens; 36 micrograms radium and one dozen radium baths in three weeks' time. At expiration of this time showed much improvement; gain in weight; amelioration of dyspepsia. Six months later continued well.

Case V.—*Rheumatoid Arthritis.*—M., æt. 72. All joints, especially hands and knees; distortion and increase in size; unable to sit down in a chair, dress himself, or go downstairs. First week sharp reaction; seventh day, "first good day;" in three weeks, after 36 micrograms radium and 12 radium baths, dressing himself every morning, coming downstairs alone, getting down in chair and up, and going out. Marked diuretic effect, interfering with sleep; also excitant. Lost sight of.

Case VI.—F., æt. 50.—*Recovering from acute rheumatism.* Patient in bed but with normal temperature; radium produced reaction with temperature 100°. Patient soon up, which the physician attributes to radium.

Case VII.—F., æt. 82.—*Sciatica.*. Headache, depression of spirits; under radium (two micrograms increased to six) in all 384 micrograms over period of ten weeks. Nurse reports enthusiastically; absence of pain and headache; much better look; more energy and able to do more. The physician reports that patient "bothers" him much less.

Case VIII.—Physician, æt. 50. *Rheumatism in hip;* painful and an inconvenience. Orthopedist, after exhaustive examination, called it rheumatism. After a month, patient reports many good days; says radium

certainly stirs him up; produces reactionary pains in other joints; distinctly diuretic; is now taking larger doses. Second report; after taking 288 micrograms over eleven weeks; thinks it has done him good because less acute pain.

Case IX.—F., æt. 55. *Chronic progressive rheumatism;* swelling of wrist; example of postponed action. After 36 micrograms radium over a period of three weeks, physician thought there was not much result, though swelling of wrist was less in a few days. Four months later reported very enthusiastic over radium; "had cured her rheumatism" and sent word to Case VIII to persist.

Case X.—F., æt. 50. Wife of physician; mild *arthritis deformans* (chronic progressive) of fingers; took 24 micrograms radium without admitting benefit.

Case XI.—F., æt. 55. School teacher; over weight; pain and lameness in hip, making it difficult to get about; some months duration; took 36 micrograms radium and one dozen radium baths; three months later writes as if benefited.

Case XII.—A peculiar affection of hips characterized by adduction of the thighs. Took 24 micrograms radium and 2 radium baths. Physician reported after several months that treatment had apparently produced an improvement.

Case XIII.—F., æt. 65. *Chronic progressive rheumatoid arthritis.* All joints affected; enlarged even to twice normal; one and a half years duration; has been lifted out of bed in morning and placed in chair where she sat until put back at night; fed for six months. Complete atrophy of muscles; contraction of ham strings; parchment condition of skin; pronounced an "impossible case" by an experienced clinician. Radium by intravenous injection; four of 50 micrograms over a period of four months. Immediate improvement showed itself; able to feed herself using both hands on tenth day. Improvement continued fairly steadily with some interruption; in three months got out of bed alone; seven months from date of first injection—having had no radium for three months, the hands and feet are free, with much more movement in shoulder and knees. There is an absence of pain in joints, but patient is troubled by a stitch-like pain in back, which intereferes with her rising or sitting up as much as would be otherwise possible. Remarkable improvement has occurred in general condition; color; nutrition of skin and hair; appearance again of perspiration in feet; gain in weight with a stimulated appetite from the outset. She is able to use a needle; the very latest developments have been (8 months after the first radium) appearance of perspiration of feet and cracking of shoulder joints. Much freer mobility of knees without resistance of hamstring; absence of pain complete; feet natural; as far as joints are concerned, could walk, but very little muscle development yet; greater degree in arms. This a hospital case, observed by five physicians.

Case XIV.—F., æt. 60. *Chronic rheumatism* with much pain; took 24 micrograms radium distributed over three weeks; well-marked improvement and relief of pain. One month later her physician reports her as marveling "that so much benefit could have followed use of what seemed merely water;" diuresis in this case.

Case XV.—F., æt. 54. *Rheumatoid arthritis.* Took 72 micrograms radium distributed over three weeks; patient had no faith and was reluctant to take. Was not observed very much but the physician said that two months later he could not get patient to admit more than an early and passing improvement. Four months after radium treatment

patient had uterine hemorrhage; polyp was removed; on further hemorrhage, scrapings were reported on adversely, and to give benefit of doubt, an hysterectomy was done and a virgin uterus removed.

Case XVI.—M., physician, æt. 57. Weight 225; inherits rheumatism; his own form is of chronic progressive type; shoulder and hips. Took 48 micrograms radium by mouth over space of six weeks. Felt that it stirred him up; was markedly diuretic; had many ups and downs as to pain. At end of four weeks better than for long time; where he could not get leg across to put on slipper can now almost shoulder the limb; marked improvement in digestion in respect to flatulency which had been very marked and annoying—an enormous appetite which he has to restrain. Verdict six weeks after, was that he was better than he had averaged and that radium had done him good. [Note:—The amount of radium seemed by no means proportioned to the case or the man; it may have been just enough to keep condition stirred up well without proportionate curative effects.]

Case XVII.—F., æt. 48. Heavy person; *sciatica* and pain in hip; under care of osteopath. Took 24 micrograms radium and one dozen radium baths over space of about two months with intermission. The physician's conclusions were that the treatment had a favorable effect. The stimulant action was noticeable and care had to be taken as to overmuch excitation.

Case XVIII.—The patient middle-aged club man; accustomed to liquor; full of fugitive pains; was well relieved by radium (36 micrograms in three weeks), which in a way took the place of liquor; six months later he wanted the physician to order radium for his wife.

Case XIX.—Physician's wife, æt. 40. Painful knee; not incapacitated; was decidedly relieved by 24 micrograms over three weeks; well marked laxative action, missed by patient after leaving off.

Case XX.—F., æt. 70. Took 48 micrograms radium over six weeks; nurse reported very enthusiastically over results. The patient reported she had no "catarrh" while taking (previously constantly complained of); influenced by results in this case, another person in the house resorted to radium.

Case XXI.—F., æt. 40. Pains in fingers; took 60 micrograms radium over space of three weeks; reported much relief, though physician remarked that he did not think much was the matter.

Case XXII.—M., æt. 28. *Chronic progressive rheumatism.* Fingers and ankles swollen; had had vaccine; when seen, dilated heart, excited action; souffle; well-marked cyanosis of nails and prolabia. Took 36 micrograms radium over space of four weeks; in ten days marked improvement. Heart down to normal dimensions, steady at 70; very much improved color. On a slight relapse became discouraged and his physician had him go to a hospital and have tonsils removed as the primary source. But, two months after leaving hospital, he again wanted radium for its tonic effect and took some. After four months is about free and in improved condition but says he will have radium intravenously in case of recurrence. In this case it is certainly open to doubt whether the cure may not be placed to radium.

Case XXIII.—M., æt. 32. An acute exacerbation of *gonorrheal rheumatism* affecting especially wrists; 36 micrograms radium irregularly over four weeks. A very undependable patient, but the verdict of his physician was that it had been of benefit.

Case XXIV.—M., æt. 30. Ball-player; arm crippled with pain; took 12 micrograms radium; was immediately better and both his physician and himself ascribed the cure to radium.

Case XXV.—M., æt. 25. *Gonorrheal rheumatism* of three or four years' duration, with remissions. This attack of six months' duration; quite crippled, swollen tarsus and toes and tendo Achillis; painful hips and shoulders; marked anemia and loss of weight; not worked for four months; vaccines and other treatment. Fifty micrograms intravenously; after reaction, first improvement in a week; in two weeks so much benefit that patient "crazy for another." Another 50 micrograms given at twenty days' interval from first; quite pronounced reaction again but in six weeks very great improvement with no swelling of foot and almost no lameness, but swelling and tenderness of clavicular joints. At this time a rheumatic iritis developed; was given 15 micrograms radium and at date of writing has been at eye hospital; improvement in joints continues; on leaving hospital reported improvement.

Case XXVI.—M., æt. 25. Very severe *gonorrheal rheumatism* of six months' duration; not worked for four months; thickening of one knee; swelling of tendo Achillis and of tarsus, pain in instep making it impossible to stand; treatment by specialist including much vaccine. Fifty micrograms intravenously; thought a little improved and wanted another. Fifty micrograms given at three weeks' interval. At six weeks the physician and himself found difficulty in seeing improvement; no change in weight but laces his shoe tighter and knee, perhaps, a little less swollen but cannot stand; therefore cannot resume work.

Case XXVII.—Elderly woman with *rheumatic arthritis*, especially affecting neck which was painful and offered difficulty in moving. Twenty-four micrograms radium over three weeks and radioactive earth effected much improvement according to both patient and doctor.

Case XXVIII.—F., æt. 35. *Infectious rheumatism* after birth of child; seven years duration. Chronic progress leading to ankyloses; knees bent to almost right angle (these have been operated on at Johns Hopkins Hospital). Right arm has very little motion (from shoulder) so that she can just get it to mouth; with left, this is impossible. Fingers distorted; some flexed, some extended. One hundred and fifty micrograms radium; three injections over space of three months. Improved after first with mitigation of pain and better nights; wanted another. Three months after beginning of treatment there is a little improvement. Is having 10 micrograms injected about left elbow. One cannot speak of much result in this case after a longer observation.

Case XXIX.—F., æt. 40. Wife of physician; had been much troubled with pain in joints; no other (objective) symptoms. The physician had tried many things but said she had improved much under radium; 36 micrograms over four weeks; it was markedly diuretic.

Case XXX.—Patient an old lady with *rheumatic arthritis* and double senile cataract. The case may be related in the doctor's own words. Five weeks from inception he writes: "There was in this case a marked reaction in the joints and muscles lasting four or five days, severe enough to keep her awake nights, attended with a slight fever and marked anorexia. This reaction was followed by a rapid and very decided improvement in all the joints so that she was soon walking about and down to the dining room (by elevator). However, coincidently with the arthritic improvement she developed a state of most intense nervousness and irritability which was most trying. From being most considerate, sweet, and patient she became utterly unreasonable, wakeful,

extremely nervous, and 'touchy.' This change of disposition was quite persistent so that I finally omitted the radium after having reduced it to 2 micrograms a day. The nervous excitation gradually subsided, so that lately she has been in that respect about as usual. After leaving off the radium, however, her joint symptoms became worse again and after a few days I resumed its use, giving 2 micrograms a day. About a week ago we were out of the radium for two days. To make up for that I gave her 4 micrograms a day for two days when starting it again. That has been followed by a moderate joint reaction, but without so far any reaction on the part of the nervous system and I have reduced the dose again to 2 micrograms daily." One week later the doctor writes: "My patient continues to gain now without further reaction, slowly to be sure but gratifyingly." Two months later: "She has improved immensely; from being practically helpless, goes out for short walks every few days, dresses herself all but her hair and except for more or less aches at night, feels fine."

Case XXXI.—F., æt. 70. Physician's mother; general arthritic pains; no objective signs; chronic; accustomed to daily dose of deodorized tincture of opium, as high as 90 minims. Ten micrograms radium given twice subcutaneously at weekly intervals. Six weeks after the doctor reports the patient had experienced relief.

Case XXXII.—M., æt. 50. Gout; right great toe swollen and tender; leg swollen; confined to bed; two previous attacks; one lasting six weeks. There is already some improvement under other treatment. Intravenously 25 micrograms radium; 12 micrograms by mouth; in four days resumed work and improvement was continuous and lasting. Twenty-five micrograms intravenously repeated in ten days; reported well on sixth week. Complaint of palpitation at night.

Neuritis and Neuralgia.

Case XXXIII.—M.; *Neuritis* of arm; of some duration and some time under treatment. Took 12 micrograms radium; 1 microgram daily; physician said patient reported entirely cured.

Case XXXIV.—F.; *Neuritis* of arm; three weeks duration with pain, tenderness, and paresthesia; 24 micrograms internally; also locally three different injections of 10 micrograms each; at expiration of ten days patient so much better she did not want the third injection. A month after, no recurrence and the doctor prescribes radium for another patient.

Case XXXV.—M., æt. 35. *Neuritis;* previous attack of neuritis eight years ago, when in bed four months; present attack seven months' duration. Severe pain in left arm requiring anodyne and making nights sleepless; arm markedly swollen; hanging at side; entirely immobile at shoulder; (has been advised by surgeon to have operation on bursa and joint); fingers glazed and tense; jaundice six weeks ago; sugar reaction in urine (also for four years). Two micrograms radium daily with radium compress; after four days swelling decidedly reduced; fingers wrinkled; bones of elbow showing; arm can be moved from side sufficiently to cleanse axilla (before impossible). After this, continued use of radium internally, of compress, and in addition three different injections about shoulder of ten micrograms of radium each. Steady improvement with rapid subsidence of pain; out in eight days; back to business in twelve days (away from business six weeks); in a month rarely pain; arm now discloses atrophy of muscle from disuse; can now

button shirt and tie scarf; marked improvement in sleep, looks, digestion, tongue, and breath (odor). In six weeks joint quite movable. Has taken 144 micrograms radium with 30 injected. In two months continued increased motion; pain absent. Six months later the patient has remained well. The arm has free though not perfect motion at the shoulder.

Case XXXVI.—Neuralgia; with postoperative conditions after excision of glands. Patient had local process in cheek; ulcerated plaques cauterized several times. Finally submaxillary gland removed by incision; histological report malignant. Injection of alcohol for facial neuralgia produced paralysis of fifth nerve. This patient had fresh scar of recent operation (two lymphatics), facial paralysis, and neuralgia. Had radium pad of 50 micrograms; scar retracted and organized unusually promptly; developed another enlarged gland; had improvement in neuralgia for three weeks with some relapse in fourth; recovered use of facial muscles; three weeks later recurrence of pain; ten weeks after commencement of treatment had taken 240 micrograms radium. In fourth month the case looks like recurrent malignant disease of jaw.

Case XXXVII.—M., æt. 55. *Epigastralgia* and chronic neuralgia radiating to arm; angina; brother of physician; number of years duration; last six weeks very severe in morning; interferes with exertion; has to stop; much belching of gas which relieves pain. Diagnosis, calcification of coronaries and angina (with bad prognosis, by prominent consultant). Heart is small, at apex second sound accented; no impulse felt by hand; nothing about aorta; no general atheroma; blood pressure 120; chronic scaling eczema of face. After four weeks (96 micrograms radium) apparent improvement; has days of entire freedom; eczema much less evident. Heart has enlarged, there is some impulse and first sound has some booming character and carries the accent. Pressure increased as high as 220; artery much fuller to touch. Pain recurring, patient left off radium. After six weeks of increased suffering, sudden death supervened.

Case XXXVIII.—F., æt. 35. *Neuritis,* arm; has had several attacks and they last several weeks. This attack quite similar to the others and for a few days used other remedies. Then radium was substituted. Took 24 micrograms radium and used radioactive earth locally. Both doctor and patient were of the opinion that the case was controlled by radium; both because of relief and short duration.

Case XXXIX.—F. *Facial neuralgia.* Took 24 micrograms radium and used radium compress without relief. X-ray showed unerupted wisdom tooth which seemed an efficient cause for the neuralgia.

Nephritis and Metabolism Cases.

Case XL.—*Interstitial nephritis marked arteriosclerosis.* F., æt. 70. Chronic invalid for some years; confined to room; increasing edema of ankles; decreased amount of urine; very marked anemia. Under radium continuously for three months, about 190 micrograms being taken. There was the most remarkable improvement; edema disappeared; urine increased from 15 to 45 ounces and maintained itself; great improvement in appetite, color, and spirits. Urea also was measured and showed increase. The patient got enough better to go out riding. The radium was omitted for a couple of months. Patient had suddenly uremic convulsions with pulse of 150 of great irregularity, and complete suppression; she seemed about to die. Radium was resumed cautiously and

her condition rapidly improved. The doctor and the family paid the greatest tribute to the treatment.

Case XLI.—M., æt. 68. *Catheter-life case.* A year previously the question of prostatectomy had been raised but decided negatively on the ground of poor work by kidneys. There was an analysis made immediately previously to taking radium. Two micrograms daily was given for a week; at the end of that time the urea and uric acid showed an increase of 50 per cent. For some reason the radium was omitted but the physician inquired some time later if the radium was cumulative inasmuch as the urea and uric acid and amount had continued to increase and the showing became quite satisfactory. The patient, however, was seized by an obstinate singultus to which he later succumbed.

Case XLII.—M., æt. 12. *Essential diabetes* with accompanying parenchymatous inflammation of the kidneys. The patient was lethargic, moped, and it was for this that the radium was prescribed in the hope of getting a stimulant effect; it was an unqualified success so that it was kept up for a couple of months. The effect on the sugar excretion was also appreciable; a quantitative analysis was not made, but the somewhat increased amount of urine was reduced to normal and the qualitative test was less marked. The patient was lost sight of.

The story of these cases recounts not much more than the simple, familiar, clinical facts of everyday practise. To some, the glamour of laboratory tests being wanting, they may appear not complete—perhaps not scientifically precise. But there is still a large place for empiricism in medicine.

Radium can reduce blood pressure, but there was no opportunity for such specific applications of it. So likewise radium has marked effects on the blood picture, but no cases of pernicious anemia or leucemia offered themselves. For the cases in general, then, observations along these lines would not be likely to add much of value. So our cases are clinical pure and simple. No doubt many will scent a strong "psychical" odor in them. In quite a proportion of the cases, however, there were decided features of an objective character, whose disappearance coincided with the general relief.

In our quest for greater socalled scientific precision in the shape of objective laboratory findings we are in danger of making "subjective" tantamount to "psychical." No doubt it is much to be desired that the highly complex phenomena of radium's action be co-ordinated. But this consummation, though devoutly to be wished, appears to be a long way off. But many disturbances of the economy of sufficient proportions to constitute a morbid state and to make a patient of a person, are purely subjective, *i.e.* divorced from objective phenomena. The disappearance of these states is no less an ostensible cure, without quibbling as to its demonstration, or classifying it as psychical.

And yet it may be that in the case of radium emanation we are face to face with a greater consonance of behavior, outside and inside the body than in all drug therapeutics put together. For radium is unique in being a force and in expressing itself by liberating energy, which in turn is capable of measurement. This idea of introducing a force into the body and more particularly in the form of a solution, is more or less puzzling because unfamiliar; but the "idée mère" of radium internally is to make the blood radioactive through the presence of radium emanation—a radioelement characterized, as all radioelements are, by its instability and its certainty of passing over, according to its

own law, into the next radioelements in the scale—this transmutation, decay, or resolution, to be attended by the liberation of rays and energy.

This idea of a force, once seized upon, not only makes the effects of radium seem consistent, but it puts radium therapeutics into the category of natural and physical means, as contradistinguished from drugs—nay more, it even links up the use of emanation internally with the use of radium for irradiation, since they both have the common purpose to produce a biological recoil on the part of the tissues.

Radium emanation we ought to challenge with three distinct interpellations: in its use there are three distinct propositions involved, viz., Does it do anything, what can it do: and can it do harm?

Those who have assumed to think of radium-emanation-therapeutics as a myth, a mere piece of emptiness, are entitled to another guess. Radiam internally is a real remedy! It is not inert! It has potentialities that make it both useful and beneficent, though its action may at times be mystifying, indeed, a bit uncanny.

It is to be emphasized, however, that we have in mind a solution of a radium salt, which alone gives an assurance of permanence and dependability. Much of the disappointment and contradiction of the past hinges on the unreliability of emanation as divorced from its parent and source, viz., radium.

What can radium emanation do as revealed in this series?

1. *It is diuretic.* This is, perhaps, the most consistent single effect of radium. The ratio is, perhaps, in seven out of ten cases. This feature may be rather rapidly produced or show in any pronounced way only after three or four weeks. It would not seem to be ascribable to direct action on the kidney because radium is not excreted to any extent by the kidney. Some investigators have altogether denied the possibility of radioactivity in the urine. A recent very reliable estimation gives (after intravenous injection of a soluble salt) a recovery of 1.88 per cent. only, after three days: most of which is on the first day. If diuresis is not to be ascribed to local action, it can be referable only to general influences, such as systemic effects or changes in the constitution of the urine.

2. *It is laxative*—not so often as it is diuretic, but in a good percentage of cases. This does not mean that it procures loose motions but only what seems ascribable to quickened peristalsis. A recent investigation of great accuracy shows that after intravenous injection of a soluble salt there was recoverable in the feces on the first day 17.9 per cent. and in four days 43 per cent. This item of excretion by the intestine has a somewhat important bearing because of the possibility of irritation. The same holds true of thorium X (the radioelement of the thorium series, which is used internally). This has been accused of doing much damage by producing congestion, hemorrhage, and gangrene with, it is alleged, resulting death in some cases.

Nothing of the sort has been observed by us. One case, however, pointed in this direction:

Case XLIII.—F., æt. 70. In the last years much pain of a rheumatic nature; enormous varicosity of abdominal veins; in last two months two outbreaks of purpura, legs and abdomen, spots size of silver dollar, now fading; took only 18 micrograms radium over space of two weeks, when an ounce of bright blood escaped spontaneously from rectum; never had had any hemorrhage. [Of course there is the

possibility of connecting this with the purpura, which however, was not active.]

Cases XIII and XXVIII, in which the largest amounts of radium were used, and that intravenously, both had, about six to eight weeks after the first injection, almost a week of colicky diarrhea; they were both in bed at the time. This phenomenon was very suggestive of the elimination of radium.

3. *It is tonic and stimulant.* Remarkable is it with what consistency one may predict that radium will make a patient look and act better. As a direct hematinic it is indisputable that radium will stimulate a pronounced increase of red cells and hemoglobin, so that cases of pernicious anemia rapidly lose their perniciousness (if we may not speak of cure). This direct effect on the blood would not, however, seem to be the whole story, inasmuch as there appears to be an independent stimulant action. Some patients have spoken of a heating influence, and in Case XLVIII, even after a long period of use, the dose had to be reduced on that account.

Case XLIV.—M., æt. 60. Physician; very nervous; had some pains and got an idea of trying radium; took 36 micrograms radium in a month's time; it was during extremely hot weather which was particularly trying to him; the verdict was that the immediate effect of the radium was to increase nervousness.

See also Case XXX for a remarkable observation along the lines of ultrastimulant effect. Even more striking is the following:

Case XLV.—M., æt. 85. Senile with marked atheroma; the senility was of the harmless variety and the patient went about the house and to meals. Radium was ordered and four micrograms given in two days; the patient became violently excited, singing and shouting; a nurse had to be retained and the patient restrained. There had never been any manifestation of this sort before and the condition passed promptly on suspending the radium.

This tonic and stimulant effect, while not to be regarded as reflecting the most essential physiological activity of radium, is, nevertheless, a very important and satisfying exhibition. It seems to distinguish radium from drugs, where the by-play is to speak broadly, depressant and harmful. Thus, to take that chief of alterants potassium iodide (this being in a measure analogous to radium) in securing our effects from the iodine we have to submit with patience to the deleterous influence of the potassium.

The effect of radium in the matter of increasing sexual vigor (a part of its reputation that is historical and on which von Noorden lays stress) has not been observed, though not specifically inquired into. One case was treated with this attainment in view:

Case XLVI.—M., æt. 40. Complete sexual incapacity for a matter of fifteen years, during which he had been under observation by a specialist; from 48 micrograms of radium over a month's period he had no change to report.

4. *Metabolism and nutrition.* Here we are approaching the copestone of the arch of radium's psysiological action. While it is true that the physiological action of radium may not have been so thoroughly studied as perhaps it some time will be, there is not much dispute as to its increasing the nitrogenous metabolism. Outside of the body it is marvelous in catalysis and autolysis and in the intensifying of fermentative and digestive processes. What it does on the laboratory table it would seem likely to repeat inside the body (which so often is not the

case), because it is present in the system in the same unchanged form.

Radium from this standpoint may be looked upon as stimulating to the innumerable ferments of the body: as supplying a goad, so to speak, to the vital processes. A corollary to this would be that it ought to be an equalizer, tending to restore the balance of forces. Very interesting in this connection are the observations on the heart in Cases XXII and XXXVII. If these observations are correct (the reporter is responsible for them) then, while taking radium, one heart very obviously increased its dimensions while the other decreased—with a correspondence of collateral signs that was strongly corroborative. Granting that the fundamental effects of emanation are on metabolism, this would give it a very wide range of applicability with which it seems proper to credit it; especially, it may be repeated, as it does not have the disturbing by-play of drugs.

Its action on rheumatism and neuritis is probably through its attacking the inflammatory conditions and promoting absorption and excretion. Bactericidal action within the body, though demonstrable to a good degree outside, is probably not to be reckoned with. It would not be surprising if in the future some relationship of radium to the ductless glands were to be made out, as for example, to the adrenals.

The effects of radium on nutrition of the skin seem to me very happy. Old skin brightens up and looks younger. In Case XIII (under observation ten months) this feature was very pronounced. At the outset, the patient could have been pronounced a mummy; the skin was atrophic and parchment-like; it is now soft like a child's. The nails commenced to grow and require attention and the feet to perspire. One observer using radium for rheumatism found an acne rosacea improve; and in an old lady (where the tonic effects were pronounced) brown spots on the face cleared up.

Case XLVII.—M., æt. 55. Apothecary; *General eczema* (called psoriasis because so scaly); two months previous treatment with arsenic; on 36 micrograms radium cleared up absolutely in three weeks.

See Case III for eczema and pruritus. A case of psoriasis of 17 years' standing, now being observed by a specialist and under treatment by intravenous injection (95 micrograms radium thus far) has shown a remarkable and immediate improvement.

In our series of neuritis and rheumatism cases the results have been such as to point to a considerable degree of control by radium over the conditions. As in so much of the task offered to radium (and this is even more true of the radiation of neoplasms) nothing is bequeathed to radium until it is wellnigh hopeless. Many of the cases have been rheumatoid with much change in the anatomy. Perhaps the time will come when radium will be offered something easier. Falta uses emanation in acute rheumatism and prefers it to the salicylates.

In general it may be said that the nearer the joint is to a "juicy" stage—periarticular or intraarticular edema or effusion, the more pleasing the prospect.

The neuritis cases have all done well. Case XXXV was really brilliant. The more of an inflammatory element the better.

As a pain killer radium has great power, but in the case of nuerotic neuralgia in highly nervous individuals the outlook is not so good.

Case XLVIII.—Fractured hip in an old withered limb; patient up and about in spite of it, but suffered much pain at night; was much relieved by radium and took it for six weeks or more; it was quite excitant.

5. External and topical. Even a weak solution (2 micrograms to 2 ounces) is anodyne. We can testify from personal experience to its instant relief of toothache; this a dentist has confirmed in several instances. Held in the mouth for a few minutes a small quantity of the same solution will produce, not immediately, but after some hours, stiffening of the mucous membrane, swelling and blanching of the lip, viscidity of the pharyngeal mucus, and it almost seemed, a little clumsiness in speech.

Saliva diluted with water will be very foul in forty-eight hours; diluted with radium solution (amount of radium 1/15,000 mgm.) it will remain unchanged a week.

Case XLIX.—F., æt. 10. After incising a fat boil on the lip (size of the tip of the little finger) I applied solution of radium (2 micrograms to 2 ounces) as a moist dressing. The boil was entirely dry, scabbed, and insensitive in eighteen hours. The patient later volunteered the information that "the scab was white."

Case L.—Ivy poisoning; the rash failed to mature and the itching was much relieved; in this case also; there was a dry white skin at the point of greatest intensity.

Case LI.—Pyorrhea alveolaris; a tooth inflamed to extreme tenderness, very loose with gum beefy and with an alveolar absess, which two dentists said would be lost, is now relatively firm and entirely serviceable. In this case a solution of radium (25 micrograms to 2 c.c.) was packed beneath the gums and this same solution was used in the nerve cavity after excavating. Solution of radium (2 micrograms to 2 ounces) was used to rinse the mouth.

In a metropolitan surgical clinic all pus cases have been treated with solution of radium (2 micrograms to 2 ounces) and the control of radium over the process has been surprising.

Chronic empyema of the accessory sinuses (cures of which by radium internally have been reported) have been treated in two instances.

Case LII.—*Purulent catarrh of the antrum and ethmoid;* a year's duration; operation advised by several observers, but refused; treated for a number of months by injection without improvement; put on radium solution internally with injection of the same (2 micrograms to 2 ounces); after four weeks the doctor reported the amount of pus in the wash water as reduced one half with the advent of what was apparently cholesterin; the patient said she felt better. For some reason in spite of this improvement (which was confirmed by nurse assistant) treatment was not persisted in.

Case LII.—M., æt. 45. *Empyema of antrum causing vertigo.* The patient, a physician, was obliged to relinquish work; absess drained and washed out with solution of radium (2 micrograms to 2 ounces). The attendant says the case did extremely well. The vertigo promptly disappeared and the patient has no symptoms. After two months there is a very slight discharge in the washings.

Dosage.—In making a radium salt form the basis of dosage, it must be borne in mind that the amount of emanation present is subject to a definite law—it cannot be more than the equilibrium quantity, which is a fixed constant. Quite otherwise is it with emanation *per se*—the amount of which present can be increased *ad infinitum.* The basis of comparison between a solution of a radium salt and a merely radioactive water (emanation) is quite unequal. For, the moment the emanation of the radium salt solution is separated or transmuted—

more will be furnished to take its place. Thus a solution of a radium salt has potentially a reserve supply of emanation which for the time being yields no units of electrical measurement.

In the preparations used in this series the maximum of emanation had already collected and thus in association with 1 microgram of radium we have one microcurie of emanation or 2,700 Mache units by measurement.

Some of the radioactive springs of Europe have an almost ridiculously small emanation strength (a few Mache units to the liter). Results have been claimed from them nevertheless. When now we turn to such doses as 1,000,000 to 1,500,000 Mache units of the London Radium Institute, no wonder that the older observers are inclined to apply the term "psychical" to their early results.

From this wide range of extremes it might seem as though there was nothing fixed about the dosage of radium. No doubt the dose is more or less flexible. The very high doses came about through the influence of thorium X, the cheapness of which gave the desired opportunity for forcing the pace. But the experience was a thorny one. Injury and death were confessed to and warned against by the very users. Since then the tendency has been towards lower dosage just as in the use of radium salts for irradiation. Moreover, the men of longest and largest experience are saying that they obtained equally good results with the small as with the larger quantities.

Our own experience in the above cases has shown that the adjustment of quantity to the case is a matter of nicety and calls for judgment.

Of the very large doses it may be said that, if radium is selective a really superfluous and unutilizable quantity may have been introduced with the bare result of a mere waste of ammunition. One has to be on the look-out, no doubt, for something corresponding to the action of radium in irradiation, viz., in one case stimulation, or absorption, and disappearance of morbid processes in another.

One puzzling part of the application of dosage is the production of reaction either to an undesirable degree or prolonged. It then becomes a nice question whether to leave off or to increase the dose.

The cases related had many of them this essential drawback, that the treatment could not be prolonged or the dosage pushed at will on account of the expense. So that in many of them, we may say there was no proper try-out and that results are merely fragmentary. The duration of a radium cure, if for well-established and intrenched conditions, ought to be from two to three months. Moreover, the maximum effect does not always coincide with treatment and there may be even a delayed improvement setting in only after cessation.

Without any question we have seen some such exhibitions. This is, perhaps, more likely to occur where a radium salt is taken, because of the greater possibility of accumulation. None can be predicted as possible with emanation simply, but only the retention of some of the later radioelements in the scale.

Proescher and Viol have shown that, following injection of a radium salt, radioactivity may be demonstrated in the organism after at least three months, and that by far the largest amount of radium may be recovered from the bone and bone-marrow, where it has been deposited in the form of an insoluble salt.

The average dose with which we have tried to work has been about 4 microcuries daily, viz., about 11,000 mache units. (In Kreuznach,

where radium treatment has been most systematic, the daily dose is from 5,000 to 15,000). A smaller dose and for a shorter period has seemed to render service in some mild conditions. It is quite clear that the attempt to crowd the dose, in a certain proportion of cases at least, may throw the patient into a decidedly upset state. There may be lassitude and a decided lack of energy or a mere state of nervousness. The experience with these cases has seemed to teach the lesson of approaching the maximum dose very gradually.

But nothing is to be expected from a low dose and short period of administering in serious chronic conditions. Thus there had been four cases of paralysis agitans which it did not seem worth while to include because there was no really serious or consistent employment of the treatment. It is to be said, however, that in two of them a stimulant action could be noted and a rally from the extreme depression. I have seen one case under much longer radium treatment in which the patient so far improved as to be able to feed himself and to go about, neither of which things was possible at the commencement.

The object being to introduce the emanation into the blood, lodging it there by the immediate route of the vein is, of course, the method *par excellence,* hypodermic or deep injections would come next and giving by the mouth last. Here, owing to the extreme diffusibility of the emanation, there is a considerable portion of it lost without passing into the systemic capillaries. Subcutaneous or deep injection gives some share to local action, although it has been shown that a soluble salt does not linger long.

Can radium internally do any harm? We have not been able to detect any traces of damage. Under the skin and intravenously there is nothing in the way of local reaction and it is certain that we can introduce into the blood good large quantities without particular reaction. Pains may be touched up, but of constitutional disturbances there is no evidence. Cameron and Proescher have given 1,800 injections of radium salts over a space of two years and in quantities up to a milligram without observing the slightest injurious effects.

Administering *per os* has perhaps one advantage, viz., its local action on stomach and digestive tract. The influence here is undoubtedly considerable and favorable.

In conclusion it may be said that this experience has served to teach that radium emanation (and the same thing is true of irradiation) calls for one requisite that makes it in a way ill-adapted to the American temperament, viz., patience. That one should attempt to disturb a profound, well-in-trenched chronic state, with a week's use of radium is as puerile as to set off firecrackers and assume to call it an assault on the citadel.

The impression which it is desirable to make, whether we are using radium externally or internally, is essentially biological, *i.e.* morbidity is to be made to reform itself by a process originating in its own baliwick. Here the initial performance would undoubtedly be to set in motion just those processes that could acquire momentum and propagate themselves, viz., a cellular recoil. In either case, within or without, radium is to be looked at as just the goad or stimulus to the self-regenerating apparatus.

At all events, the radium question is here and it will be settled and settled right. That will take time and a heap of patience. To this end open mindness is a great desideratum. Above all, systematic use of it after every fashion on an ample scale is to be hoped for. To be

this, in respect to emanation, the above series could, of course, scarcely make claim, but as an initial try out it may prove of interest and we hope a little importance.

39 NEWBURY STREET.

REVIEWS AND ABSTRACTS.

John G. Clark, M.D. (Philadelphia). What Do the Newer Methods of Treatment Offer the Patient With Malignant Disease of the Uterus? N. Y. Med. Journ., Sept. 4, 1915, pp. 485-487. "From time to time new remedies or 'cancer cures' have appeared on the medical horizon, engendering hope as to their therapeutic possibilities, dazzling us for the moment with their cometlike splendor, only to sink into oblivion, never to reappear during our generation."

"In the continental literature of three years ago surgery was the only method of treatment considered; suddenly, however, a wave of enthusiasm swept over France, Germany, and, to a lesser degree, conservative England, and radium became the subject for extended discussion in the literature. From the pinnacle of surgical exaltation the scene shifted, and some of the strongest advocates of radical treatment turned abruptly from the enthusiastic laudation of surgical measures to the advocacy of mesothorium and radium. Thus in the space of two years we find Kroenig, of 'twilight sleep' fame, who, in the last review of his ultimate results in the clinic at Halle, held that, instead of limiting the extent of operative indication, they should be broadened so as to encompass a larger number of cases hitherto considered inoperable, veering away from surgery, and acclaiming mesothorium and radium as the great panaceas. Such enthusiasm must be counterbalanced by the conservative physician, for undoubtedly there is a vast deal of good in both measures. Startling assertions in favor of the potency of mesothorium and radium were made, and, what was more astounding, these assertions were apparently sustained by the report of a long series of cases studied accurately from every side. The clinician pronounced the disease a carcinoma of inoperable extent; the microscopist confirmed the diagnosis; and radium was then applied, and soon a remarkable transformation was observed; usually the hemorrhage and offensive discharge ceased, and the local areas of ulceration underwent cicatrization. The cancerous tissue either disappeared or showed evident signs of degeneration, and microscopists confirmed these retrogressive changes in the malignant cell and observed a regrowth of healthy tissue. With it all, however, even the most enthusiastic followers of the new method cautioned against the abandonment of surgical procedures in favor of this newer agent, and this is precisely the position we occupy today, even after three years of active use, upon the continent, of the radioactive substances in the treatment of malignant growths."

"Schauta, of Vienna, who has made a careful but conservative study of these cases, gives an excellent summary of the effects of radium, and of what may ultimately be expected from it. In his discription of results he says:"

"The nodular masses covering the cervix disappear; one may also say that they melt away, as ice before the sun. The rigid, resistant,

easily bleeding walls become soft and smooth; in many cases the formerly unrecognizable portio vaginalis assumes again its original contour. A distinctive elective action is noticeable in all these changes; in no instance was the vagina in any way inflamed; there was no necrosis produced, not even a reddening or desquamation of the epithelium could be noticed. At the end of the treatment the line of transition from carcinomatous tissue to healthy vaginal wall is generally marked by a circular wall of connective tissue in which no carcinoma is to be found, a more or less well marked crater indicating the site of the former cancerous growth. Microscopic examination of the excised bits of tissue showed, often after the first or second application, at the latest after the third, no unaltered carcinoma, but only swollen, degenerated carcinoma cells, or none at all."

"In addition to these local effects, however, again to quote Schauta, he encountered quite marked general reactions, such as headache, loss of appetite, gastralgia, enteralgia, alternating constipation and diarrhea, pain in the bladder region, and temperature elevation. Except in a very few cachectic and seriously ill patients, these symptoms always disappeared within twenty-four hours after the radium tube was removed, and no permanent injury from its use could be demonstrated. In a few instances quite severe hemorrhages occured, probably the result of destruction of tissue by the action of the radium."

"In one case a vesicovaginal fistula, and in another a rectovaginal fistula resulted. These were probably due, not to any destruction of healthy tissue by the radium, but to the fact that the respective septa in question were completely infiltrated with carcinoma, and as these were destroyed by the radium, a fistula naturally resulted."

"As regards the indication for the employment of this agent, Schauta considers every case of carcinoma a suitable one for radiotherapy; for the present, however, he declares that he will continue to employ surgical measures on all operable cases, as permanency of the apparent radium cures has not as yet been established; after all operations, however, he will apply moderate doses of radium as a routine to ward off possible recurrences."

"Another report that runs along similar lines is that of Exner, who for ten years has used radium in the treatment of malignant growths, getting splendid results in the case of superficial, but very unsatisfactory ones in the more extensively involved cases. Of forty cases so treated, two which were apparently cured remained so for from seven to nine years, when recurrences developed and they ended fatally. He believes, however, that the lives of all the patients were prolonged, and the majority rendered more comfortable, but he does not aver that a cure was effected in a single case."

"Wertheim, one of the sponsors for the radical method of operation, has employed radium in nineteen cases of uterine carcinoma. None of these was in the operable stage, one was a borderline case, and nine cases were absolutely inoperable. In seven of the operable cases a hysterectomy was performed after the application of radium had been made. Specimens removed showed that decided destructive effects had taken place in the carcinomatous cells, but he asserts that a complete disappearance of the tumor was not observed except where the growths had been superficial. This observer believes that similar effects may be accomplished as the result of cauterization or of amputation of the cervix. Speaking from his personal experience, he does not believe

that there is sufficient evidence to warrant the assumption that the radical operation is to be displaced by radium therapy."

"At the International Medical Congress held in London in the summer of 1914, two French observers, Cheron and Duval, reported the results of 150 cases of uterine and vaginal carcinomata treated with radium during the past five years. These writers believe that the unfavorable results reported in the literature were due to a faulty technic in the administration of the radium. They laid particular stress upon efficiency of massive doses well filtered. In their opinion radium given in small doses ranging from ten to twenty mg.—is worse than useless, in that the remedy may actually stimulate the growth of the tumor cells. Similar reports have emanated from the London Radium Institute."

"From the literature here reviewed we must inevitably draw the conclusion that radium offers excellent possibilities in the treatment of superficial growths and is useful for the relief of hemorrhage and to lessen the offensive discharge in extensive cases, but that no extreme degree of optimism can be gathered from these reports, since they all point to one fact, namely, that the deeper metastases are not reached by the radium, and that, therefore, the fate of the patient hangs upon this one point. This is a somewhat interesting observation, since it tallies so completely with our own surgical observations in the treatment of carcinoma of the uterus. We have long since abandoned the extensive dissection of lymph glands, and, from my personal observation of cases coming under my care, I reached the conclusion, five years ago, that when the deeper iliac glands are the seat of metastases, we are merely fighting wind mills, so to speak, in the attempt to cure these patients. Since that time it has been my controlling policy merely to remove one or two glands for microscopic examination. When a radical operation has been performed and these glands are demonstrated to be free from cancer, the prognosis is guardedly favorable. Conversely, if metastases are found, no hope for ultimate cure can be held out."

"THE X-RAY IN CARCINOMA OF THE UTERUS. Because of the great expense of the radium treatment, attempts are being made in all countries to achieve good results with the X-ray as could be secured from the more expensive form of therapy. Perhaps the most thorough report on this subject comes from Professor Bumm, of Berlin, who has endeavored to perfect a method of treatment by the use of the X-ray. He believes, that, eventually, the Roentgen ray will prove a very effective substitute; indeed, he is inclined to predict that this latter agent will supercede radium in the treatment of uterine carcinomata. In his opinion a technic will be evolved to permit of satisfactory treatment with the X-ray, without resulting serious burns of normal tissue. He even makes the startling assertion that, with the use of the newer tubes, it may be possible ultimately to reach these cases without the necessity for employing vaginal treatment. In order to prove his theory, Bumm subjected six women suffering from advanced carcinoma of the cervix, in all of whom large, fungoid, freely bleeding masses completely filled the vaginal vault, solely to radiation from the abdomen or back. In all these cases the tumor disappeared completely within a few weeks. Specimens of tissue excised for microscopic examination showed almost complete destruction of the carcinoma cells, only a few scattered, degenerating remains being found, and these surrounded by dense masses of fibrous tissue. In one instance, no cancer cells were demonstrated."

"From these experiments Bumm believes that many deeply seated

growths hitherto regarded as of unfavorable prognosis may be offered a hope of cure by the use of the X-ray. The technic must be very carefully carried out, however; moreover, the method requires time and is costly, facts that must be recognized by physician and patient. This observer draws attention to the fact that in many instances considerable irritation of the skin is bound to result, and this may even go on to the formation of blisters. This dermal condition, he states, will rapidly disappear under local treatment, and, in his opinion, is a very slight objection when compared with the ultimate cure of an otherwise hopeless malignant growth."

"Out of this mass of literature reviewed by us, we arrive at the inevitable conclusion that the X-ray in these large doses must possess harmful effects upon normal tissues, and prove an actual danger from deeply seated burns. Kroenig, one of the most enthusiastic exponents of the use of mesothorium and radium, does not, as previously stated, aver that a single cure of cancer in which there were deeply seated metastases has been effected. Basing our statements upon the literature and upon our own limited experience in the use of radium, we should set down as definite postulates the following conclusions:

1. "Up to the present there is not sufficient evidence in favor of radium to justify one in using it as a substitute for surgical measures in operable cases."

2. "As a forerunner to and a follower up of an operation, it is unquestionably advisable."

3. "In inoperable cases it should invaribly be tried, for apparent cures have occured in some markedly advanced cases, and in those cases that are not ultimately cured there is, nevertheless, a decided amelioration of symptoms—in many instances, the offensive discharge and hemorrhage completely disappear."

4. "A serious disadvantage in the use of radium is that it occasionally produces a widespread necrosis, leaving vesical and rectal fistulae in the wake of its destructive action. This, however, usually occurs only in advanced cases of carcinoma, and need not, therefore, deter us from the use of the remedy."

"CHEMOTHERAPY. From time to time chemical means for the cure of cancer have been advocated. Thus far, however, no measure has proved of sufficient value to be accorded more than a temporary place in the literature, and, therefore, this subject may be dismissed without further discussion."

"The treatment of carcinoma by cancer extracts and various serums has also proved to be worse than valueless."

"THE TREATMENT OF INOPERABLE CARCINOMA BY HEAT. In this country a very ardent advocate of dessication heat for the cure of carcinoma is Percy, of Galesburg, Illinois. This investigator is of the opinion that experimental work has proved that cancer cells may be destroyed when the temperature of the affected part is raised to between 50° and 55° C. For the purpose of applying heat to inoperable carcinoma masses he uses a 'cold cautery' at a comparatively low degree of heat for a sufficient length of time to destroy not only the superficial, but also the deeply seated growths. He has not as yet published a report of a definite series of cases treated by this method, and thus far his experiments have been conducted largely upon a theoretical basis. He maintains that he has had most remarkable results in individual cases, but as these are but isolated examples, it seems that no proper estimate of this plan of treatment can be made until a careful

detailed study of the cases is presented. In justice to Percy, however, it must be said that the majority of surgeons in the United States who are attempting to use his method, have started in on the assumption that he employs cauterizing heat. He protests very strongly against this use of his cautery, and prefers to speak of it as a 'cold cautery.' '—' Much credit is due him for having elaborated this method, and where radium is not available, I consider it the duty of every surgeon to equip himself with this apparatus."

"From my own experience, however, with the use of radium, I feel that this agent affords better, at least equally good chances for cure without the attending dangers of mortality incident to the operation proposed by Percy."

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Russell H. Boggs, M.D. (Pittsburgh). Radium and Mesothorium in Conjunction with Roentgen Therapy. The American Journal of Roentgenology, April, 1915, pp. 831-736. "All Roentgenologists realize the value of radium, but there is much difference of opinion in regard to its exact uses and limitations. Some will say they are unable to see any difference between radium and Roentgen ray reaction, while others will say that there are certain things that can be done with radium that cannot be done or at least duplicated, with Roentgen ray. Nearly all agree that certain lesions can be treated just as well with one agent as with another. There is no question among the physicists that radium and the Roentgen rays have certain differences, but that each contains certain rays which are analogous."

"It is not my purpose to attempt to describe the physical properties of radium, mesothorium or the X-ray, because my paper pertains to the clinical side of the subject."

"It is generally admitted that the action of radium and mesothorium are the same. Most authorities who have worked with both claim that they observed practically no difference in the results accomplished. They all agree that the radio-active substances should be as highly concentrated and used in as small containers as possible as the penetration is deeper."

"From a clinical standpoint, I believe the penetration, method of filtration and accessibility of application, more than the agent employed, determine the results in nearly all diseases which have been treated by the Roentgen rays and radium. Of course, radium or mesothorium are supposed to have about ten times greater penetration than the present Coolidge tube. There are only a few lesions where such high penetration is needed or used; because, even when treating with radium, most lesions are so situated that authorities advise using filters, which allow lower rays to pass, which predominates, and then the reaction is produced by this radiation."

"From the results produced by radium on angiomas and conditions closely allied to these tumors, such as flat naevi or port wine stains, it would appear that the endothelium of the blood vessels is more sensitive to radium than the Roentgen ray. Although Pusey states that he can even duplicate the results of those which even obtained in the treatment of vascular naevi by the Roentgen rays."

"An advantage of radium frequently mentioned is that a dermatitis of the same degree heals up much more quickly, when produced by radium than by the Roentgen rays. In one or two cases in which I applied mesothorium, a dermatitis with a marked vesiculation occurred,

and I was greatly surprised how promptly each healed without leaving a scar. I was rather inclined to think that it might be due to the small area involved, instead of the different quality of radiation. This is a point I cannot decide at the present time, for you all know that we have produced dermatitis of a marked degree with the X-ray, and were surprised at how promptly it healed. It has been pointed out that when the gamma rays (filtered through two millimeters of platinum) produced a marked reaction, less fibrous tissue seems to be subsequently formed, than when a reaction of the same degree is produced by rays filtered through one-half millimeter of platinum. I believe for the last few years the most of us have been treating keloids with as high a penetrating X-ray as possible, because results can be produced quicker with less amount of radiation. Then would this indicate that the high penetrating rays have a more marked effect on fibrous tissue than the low penetrating rays?"

"The therapeutic value of radium cannot be rightly appreciated if it has not been studied with a sufficiently complete and varied range of filtration. It is very necessary to study secondary radiation produced by the various filters and the best methods of avoiding the deleterious effects of these rays."

"In treating a case either by radium, mesothorium or the X-ray we always face a series of problems. Given a case with a certain lesion, its position, its extent, its susceptibility to the influence to this or that radiation, and then we must determine the agent or agents to use. The duration and method of application can be varied almost to infinity. This enables us to realize how rich radio-therapy should be in its results when properly selected and employed."

"There have been so many ridiculous statements made by men of high standing about radium, for and against it, that the general medical profession has no clear conception of its real value."……

"It means nothing when some enthusiastic advocate of either radium or the X-ray states there is no doubt that one agent has destroyed cancer whereas the other completely failed. Most likely the one applying the agent failed to recognize the limitations of his therapeutic agent. No one should expect to obtain the same results in cavities with X-ray alone as with radium or mesothorium, either alone or in conjunction with the X-ray."

"I have seen cases made worse by destructive doses of radium, which probably would have been avoided if the after treatment had been just as radical as the first. Many advanced cases often warrant massive radiation but the after treatment must be carefully carried out. Here is a case to illustrate:

"Mr. C., was referred after having consulted three of the best surgeons in the country. He had an epithelioma situated back of the ear about the size of a half dollar, with some glandular involvement. He had been told by the surgeons, whom he had seen that on account of his age (but in reality on account of the advanced condition of the disease) they would advise either X-ray or radium. Before he returned home he was given a massive dose of radium over the lesion. In three weeks there was a violent reaction which later became necrotic. I gave him X-ray treatment over the adjacent metastatic glands, covering the lesion with tin foil, which reduced them rapidly. As soon as the lesion became necrotic I strongly advised the removal of the necrotic area as the man was still in excellent health. But the surgeon objected to any such procedure, and said that the radium had only made it worse,

and that, as the X-rays had some effect on the glands, wanted the original lesion treated with X-ray. This I did not do as it would only have been like giving more radium. If the necrotic area and the unhealthy surrounding tissue had been removed and a flap turned in, the man's life should have been made comfortable at least."

"In consultation, I saw two similar cases in which X-ray treatment had produced the same result, one, in which the necrotic and degenerative area was removed and a flap turned in, and the other frozen with carbon dioxide. Both are apparently well at the present time. We must be able to differentiate between an epithelioma and degenerated X-ray tissue. I have frequently been called in consultation to see why the X-ray was not effective in the treatment when perhaps the physician was treating degenerated X-ray tissue, while the removal of all this tissue and the turning in of a flap often effected a cure. Experienced Roentgenologists today are not producing such conditions but are seeing the condition after it is produced."

"Hearing Charles Allen Porter's talk before the American Roentgen Ray Society in New York made me realize that, often the failure of an epithelioma to heal up was due to treating X-ray degeneration instead of an epithelioma. This fact has been very valuable to me in advanced cases of epithelioma. What has been said in regard to X-ray degeneration, I am sure, from what I have seen will apply to radium. However, I do not believe that we will have so much radium degeneration as there are not as many radium or mesothorium tubes scattered around as there are X-ray machines."

"All types of epithelioma of the skin, I believe, can be treated just as well with the X-ray as radium. Certainly superficial epithelioma is in most instances promptly relieved by both forms of radiation. Those who have had the most experience with radium think most of it and the same holds true with the X-ray. It is only necessary for the operator to be familiar with his agent."

"But where the epithelioma is situated on mucous membranes in cavities, the same does not hold true on account of the inaccessibility of the X-ray and the ease with which the radium can be applied. Pinch states that 'epithelioma of the bucal, lingual and pharyngeal mucous membranes still prove both refractory and disappointing in their response to radium, but a new method of treatment has recently been devised, which in instances of cancer of the tongue has given distinctly encouraging results; it consists in the burying within the carcinomatous nodule of a very small but intensely powerful radium tube. 'A fairly severe reaction follows,' he says, 'and in some cases the nodules cease to grow and become replaced by dense fibrous tissue.' "

"I have seen Abbe carry out this method but I do not believe we can expect much from it. An advanced case of cancer of the tongue is not a local disease, and what we need is a homogenous ray to check and obliterate the disease in the glands. In the advanced cases I have been able to check the progress and make the patient comfortable but have only one case which has been apparently cured for any length of time. On account of his remaining apparently cured I question the diagnosis. However, I believe he has not taken any treatment of any kind for over three years. If epithelioma of the tongue is seen early when the diagnosis is hard to make, there is a number of methods which will effect a cure, particularly so if the adjacent glands are treated by some effective form of radiation. But when the patient comes late,

it is probably the most hopeless form of carcinoma and the one for which we can do the least."

"Leukoplakia is usually a forerunner of epithelioma and responds more readily to radium than to any other method I have tried or seen. I have one case of tuberculosis of the palate under treatment that responded to radium promptly. The X-ray, on account of its inaccessibility, would not have been effective. I treated the external glands with X-ray, a procedure which I have adopted since I have been using mesothorium in diseases of the mouth and the throat. This is just as important as the removal of the glands and raying after operation for carcinoma of the breast."

"Carcinoma of the breast is one of the most common forms seen by the radio-therapeutist, and one over which there has been more discussion, for and against, than any other form of cancer treated. When patients of carcinoma of the breast are told the truth (so too much is not expected), I believe that this is the most grateful class of patients we have treated by radio-therapy, because so much can be done and in the hopeless cases so much relief is afforded."

"Pinch's report of the radium institute shows that 128 cases of mammary carcinoma applied for treatment in 1913, which far exceeded that of any other malignant condition. His policy is still rigidly adhered to in declining to treat operable cases just the same as the Roentgenologist. In speaking of carcinoma of the breast he states that, 'many patients exhibit a great susceptibility to radium; the primary growth becomes smaller, infected glands and subcutaneous nodules lessened or perhaps even disappeared and that little or no effect appears to be exerted in prevention of metastatic deposits, though the treatment has not, at any rate, hastened their dissemination.' This is one place I believe where the Roentgen rays are superior to radium, and I am sure that the X-ray does check metastases while Pinch in the above quotation claims radium does not. Even if radium had a greater therapeutic effect than the X-ray, the latter is preferred in any form of carcinoma of the breast on account of the great mass of rays that can be poured into the body, giving large doses to more distant parts. In the future, this statement may have to be modified, providing radium is available in sufficient quantities. On account of the lymphatic supply being so great and so widely distributed, it is necessary to radiate the whole chest and mediastinum with high penetrating rays, using the cross fire method; that is, applying the rays from the front, back and side at different angles."

"Radium or mesothorium is a very useful and at times necessary adjunct to Roentgen therapy, in treating carcinoma of the breast, as a radium tube can be placed in the axilla, where X-ray is difficult or impossible to apply in many cases, particularly after operation. During the past eight months I have adopted this method whenever possible, and, without going into detail, it acted like a massive dose of the Roentgen rays. In some cases I have applied a tube of mesothorium over the supra clavicular glands because it is often difficult to keep a nervous patient still in the proper position while giving Roentgen therapy. This was before I had been using the Coolidge tube."

"The treatment of fibroid of the uterus and cancer of the uterus and rectum by radium and the Roentgen ray is large and very important subject, and my experience is so limited compared to some of our members' and to many European authorities' that I shall only mention this subject here in order that fuller discussion may follow. Every

one here is familiar, at least to a certain extent, with the work done in the clinics of Kroenig and Gauss, Albers Schoenberg, Bumm, Doderlein and others. The symposium of Pfahler and Kelly at the last meeting of the American Medical Association in Atlantic City will do much toward enlightening not only the general medical profession, but many of the Roentgenologists who have neglected this very important subject."

"In the treatment of fibroids of the uterus, I have used Roentgen rays alone up to the present time, while in carcinoma of the uterus, as a prophylactic measure, and in inoperable carcinoma of the rectum, I have been using mesothorium locally and the Roentgen rays by the crossfire method externally. The general opinion of rectal carcinoma is that the disease displays great variation to ray therapy; often a proctitis occurs, which is usually transient, but sometimes persists and adds greatly to the discomfort of the patient. In one case in which this occurred, the symptoms were relieved by a suppository containing five grains of iodoform. It has been noted that when the growths are situated low down there is always more tenesmus than when in the upper half of the rectum. In some instances before inserting the tube, I have found it necessary to give the patient an injection of morphine. I have a case now where the surgeon intends to make an artificial anus so that the irritation of the feces will be avoided. He feels sure that then much better results can be obtained. Temporary results have been marked; that is, pain has been relieved and the mass has been reduced. Two cases that improved, in which the distressing symptoms disappeared and the mass became smaller and more freely movable, were operated upon. One is in good condition and expects to continue the treatment, the other case developed a rectal abscess and was unable to return for treatment."

"The results in inoperable and recurrent carcinoma of the uterus have been gratifying, in that the local manifestation of the disease has been benefited in a striking manner. Checking of hemorrhage and discharge and relief from pain and the healing of ulceration with a reduction in the size of the mass in a large percentage of cases have been observed. In some patients the relief of these symptoms is only temporary, while many authorities have shown, by using radium locally and X-ray externally, a certain percentage of apparent cures have been obtained. I treated a case four months ago where there was a recurrence after hysterectomy. Upon examination thee weeks ago no evidence of the disease could be found. We expect to give more treatment. The results which have been accomplished in deep seated malignant growths have been the means of inducing a few surgeons to refer patients for radiation after hysterectomy."

"In conclusion, it should be stated that there is some confusion in the minds of many in regard to the limitations of radium and Roentgen therapy. It is generally conceded that certain lesions can be just as well treated with one agent as with the other. Many authorities conclude that the only places where radium is superior to the Roentgen rays is in its accessibility in cavities and in its greater penetrating power. Most lesions are so situated that rays so penetrating as those of the high gamma rays are not neceseary for the best possible therapeutic results. We know that the high X-rays give, in a majority of cases, results quite as good as those obtained from radium."

"The reason why the X-ray has maintained its place in the treatment of cancer is not merely on account of the difficulty of obtaining sufficient radium; but it has the advantage of being administered in

a fairly uniform depth, whereas, the radiation from radium is only effective within comparatively short distances. This, in carcinoma of the mouth, esophagus, rectum, cervix, etc., radium should be preferred for the treatment of the primary growth, although X-ray is necessary in the treatment of the lymphatics draining the part. In other words it is impossible to treat large areas homogenously by radium."

"If radio-therapy was employed only as a prophylactic routine measure, many lives would be lengthened and many recurrences prevented. Rapidity of development of the growth is no contra-indication to ray treatment, although the dissemination of the disease is more rapid and even when the local growth disappears recurrence in distant parts is more common. At the stage at which malignant growths are referred for radio-therapy it is true that only a small proportion of the cases get well but no other method even offers any hope of relief. Experience of a number of years has taught Roentgenologists to look for temporary improvement in the treatment of malignancy as a matter of course. For instance, anything from one to three years' prolongation of life is the usual and is almost the rule in hopeless and recurrent cases. We are accustomed to see recurrent growths disappear in a few weeks, with complete restoration of health. When such results are produced by radium they are looked upon as marvelous, chiefly because they are now seen for the first time by physicians who had no previous belief in the efficiency of ray therapy in any form, but now progress is coming about by the co-operation of the surgeon and the professional radio-therapeutist, when the proper ray is selected for each case."

"Finally, radium therapy is the method of choice in carcinoma of the rectum, vagina, uterus, axilla, etc., but even where the X-ray forms a useful adjunct so far as the adjacent parts are concerned. The rays from both radium and the X-ray affect certain cells more than others, lymphoid tissue and the endothelium of the blood vessels being first affected. All cells that are undergoing rapid reproduction are more readily affected han where the reproduction is normal. Tumors rich in blood vessels and spreading by the lymphatics are checked in three ways: first, by the action on the epithelial cells, second, the endothelium of the blood vessels undergoes proliferation until the lumen is almost obliterated, and third, the channels or lymphatic glands are blocked, preventing metastases."

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Walter B. Chase, M.D., F.A.C.S., (Brooklyn, New York). Radium in Gynecological Practice. The American Journal of Obstetrics, July, 1915, pp. 90-97. Read before the Seventh Pan-American Congress, San Francisco, June 17-21, 1915. "Watching and participating in the unequal struggle for the mastery of malignant growths by excision, the writer believes with many other operators, that surgical procedure has apparently reached the limit of palliative and curative power, and while holding to the principle that large operable growths belong to the domain of surgery; that surgery and radium are not incompatible, but in their utility reciprocal and supplemental."

"The efficacy of radium rests on its occult power to inhibit lawless cell proliferation and destroy cancer tissue. The law of reaction is the governing factor in its use, and only by mastery of this art can success be attained. It is assumed a given amount of radium applied at the same distance with the same screening will produce the same results if the tissues, to which it is applied, normal or malignant,

possess the same resistance. When lack of uniformity in curative results is found, the inference is unmistakable that the individual resistance of the patient's tissues is a controlling factor in radium therapy. Knowledge of such resistance can only be determined by actual application. This principle has been demonstrated to my satisfaction as being clinically and logically correct, and is apparently the only natural and rational explanation, why one case is cured by small dosage of radium, while another is irresponsive to several times the quantity. The mastery of the art in the application of radium is only acquired by observation and experience, and must be applied in every case, before results can be tested or predicted. In this paper I shall state some of my experience and report a few of my own cases, together with the experience of American and European authorities."

"The treatment of uterine cancer, whether curative or palliative, is a matter for clear and discriminating judgment, as its operability hinges on the degree of parametric infiltration and the extension and location of lymphatic metastasis. If inoperable, it belongs to the field of radiumization. This has its limitations. Too small quantities stimulate malignant growth. Too large quantities may perforate hollow organs, blood-vessels and irreparably injure nerve trunks causing destruction of both malignant and normal areas of tissue, as was proven in von Eiselberg's clinic in Vienna. The palliative function of radium affords dimunition or arrest of pain for days, weeks and sometimes months, and gives a new lease of hope to the unfortunate sufferer. I note two cases of its analgesic power."

"Case 1.—Mrs. K. A., aged thirty-two, of New Jersey. Advanced inoperable carcinoma of entire uterus—suffering hemorrhage, cachexia and great exhaustion—taking opiates. Commencing September 14, 1914, radium was used twice a week. In less than a month pain was almost absent, hemorrhage controlled, appetite and strength much increased. From this time on, until three weeks before her death in January, 1915, she was almost without pain."

"Case 2.—Mrs. D., aged seventy, widow, mother of four children. Came under my care February, 1911, with cervical carcinoma of the cauliflower variety. She was weak, cachectic, with a prospect of living six or eight months. She had three thermocautery operations— each followed by the use of radium; after the second operation healing took place—recurrence followed and radium was used with partial healing. She remained in comfortable health and without pain until January, 1915. It is quite safe to affirm three years of comfort were added to her life."

"For ten years it has been my practice in cervical cancer to do the high thermocautery operation—and destroy the endometrium by doming the body, followed by radium. Experience confirms my belief that it is the most efficient method of treatment except as hereafter mentioned."

"Panhysterectomy in all malignant conditions of the uterus is the remedy par excellence before metastasis renders it futile. The particular form of operation rests with the operator."

"It will be noted that radium therapy is based on prophylactic preoperative and postoperative application. To insure the highest degree of efficiency its early use is imperative. A large percentage of postoperative radiation, is deferred weeks or months after metastasis has appeared. The most favorable time for application is immediately subsequent to operation. Another requirement must be kept in view,

namely, crossfire with radium, which greatly enchances its power, when anatomically possible. Not infrequently burying radium in malignant structures or placing it in the vagina is of the highest importance. In uterine cancer I have so used it continuously for a period of ninety-six hours."

"Cancer of the vagina, clitoris, and labia yield to radium rather reluctantly, as is true of all mucous surfaces. It is oftentimes well to subject such growths to the influence of heat by the thermocautery and follow with radium. The bladder and rectum, so contiguous to the uterus, with or without involvement of that organ or vagina, are within the domain of the gynecologist, as are the uterine adnexa."

"Not alone in malignancy has radium a field of application in gynecological practice. Its power to control uterine hemorrhage is worthy of trial and consideration. Later it is my purpose to report my experience."

"Without attempting a resume of the several features under discussion, particular emphasis should be given to prophylactic radiation. Its analgesic influence in affording palliation and sometimes a controlling influence over pain with avoidance of perturbing opiates, is one of its most precious properties, almost unknown and little appreciated. Insistance on the utility of crossfire frequently by burying the radium in malignant growths has too long been neglected."

"The writer is impressed with the belief that too little attention is paid to the general health and the hygienic surroundings of the patient. Finally, as in surgery, so in radium, disappointments are and must be encountered, and caution should be exercised in making promises as to results.

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"Radium and X-Rays as Complements to Surgery in Lymphosarcoma.—Two cases of lymphosarcoma of the neck, in which incomplete ablation was followed by radium and X-ray treatment, are described by Begouin (Arch. d'electr. med., June 25th, 1914). The observations are of too recent a date to permit a definite judgment as to the ultimate value of the treatment, but the result was so different from the usual sequel to an incomplete operation as to justify reporting. The first case was that of a woman, aged 45 years, with a tumor slightly below the midcarotid region, taking the size and form of an elongated orange. A surgical intervention was made by means of a long incision on the border of the sterno-mastoid, and the tumor proved to be a ragged encephaloid mass, which bled freely. It had infiltrated the sternomastoid muscle, and penetrated the environing interstices in such a manner that, the principal mass being removed, there remained on all sides an inextirpable neoplastic remainder. The operation, therefore, was necessarily incomplete, the skin was sutured, and a drain was left in place in the lower part of the wound. In this drain, four days after operation, a tube containing 18 cg. of pure radium bromide, with a silver filter 0.3 mm. in thickness, was left in place for twenty-eight hours, and a further application similar in character was made for eight hours to a different part of the cavity a few days later. Afterwards, the cicatrization of the wound being complete, the patient was submitted to intensive X-ray treatment, strong doses (8-9 H.) of very hard and heavily filtered rays being given. These irradiations were repeated at various ports of entry at intervals of a few days, at first directly on the site of the tumor, and then indirectly to traverse the neck. The histological examination of the tumor had proved it to

be a lymphosarcoma, and, judging by other cases, if recourse had been made to surgery only, the removal being incomplete, a relapse would have been immediate. Eight months have passed since the intervention, and the operated region remains supple, with no tumefaction or trace of relapse, and the general health is perfect. The author brings forward a similar case in a woman aged 60 years. The mass of the tumor was again removed in order to facilitate the action of the radium. The tumor had the same encephaloid aspect as in the preceding case, and was pronounced a lymphosarcoma. Radium was applied, producing neither reaction nor suppuration, and was followed by intensive radiotherapy. Treatment in this case was undertaken only three months before the publication of the report; up to that time, however, there was no sign of relapse, nor any trace of generalization." Brit. Med. Journ. May 8, 1915. p. 38.

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In a Symposium on Tumors of the Bladder With Special Reference to the Technique and Post-Operative Results, the following remarks concerning the use of radium were made: Papers presented at the annual meeting of the American Urological Association, Baltimore, April 13-15, 1915. Surgery, Gynecology and Obstetrics, August, 1915, pp. 135-179.

J. Bentley Squier, M.D., F.A.C.S., New York. Radium Versus Surgery in the Treatment of Vesical Neoplasms. pp. 176-78. "Surprising it is, therefore, that even though ten years have elapsed since the application of radium to the treatment of malignant tumors, certain fundamental information concerning its therapeutic capacity is still lacking. One explanation of this seems obvious; namely, that our knowledge of the real cure of cancer will depend upon our knowledge of the real cause of cancer, and the finality of one will absolutely depend upon the accuracy of the other."

"It is not at present known what quantity of radium must be applied to kill a cell of a cancer within a given distance. It is perfectly certain that in the benign epitheliomata of the face, including many types of basal-cell epitheliomata, radium is capable of inducing a cure, since there are already a sufficient number of observations on human beings to enable us to make so positive a statement. We do know that radium will not cure a carcinoma or sarcoma at a distance of, say, three or four inches from the tube. This has been shown by the work of Kroenig and Gauss and Bumm in Germany, who have published a series of cases of carcinoma of the uterus which have shown recurrence at a considerable distance from the site of the radium application, even though the primary carcinoma in the uterus had been completely destroyed. As far as one can judge it is useless to expect any effect from the quantities of radium now available at a greater depth than about two inches from the tube. Within this distance it is often possible to influence tumor growth, but the quantity of radium required is so large that but few have the necessary amount. By large quantities is meant four or five hundred milligrams, which at the present market price is worth sixty to seventy thousand dollars. The application of these large quantities, however the radium may be protected or screened, frequently results in serious burns of surrounding tissue which do not heal for a long time. Therefore extreme caution in application is necessary when applying radium to vesical tumors."

"It is well known that many of the bladder papillomata are benign or at least not extremely malignant. If such growths can be approached

either from the urethra or through a suprapubic incision and the radium placed in contact with the base in quantities of 200 mg. and for an exposure of twenty-four to forty-eight hours, there is no question but that a good deal of effect may be secured within a radius of two to three inches from the site of application. The danger of deep ulceration with the production of rectovesical fistulae or fibrosis, must, however, always be kept in mind and guarded against."

"In the malignant tumors of the prostate, involvement of the rectum or at least close approach to the rectal wall is not infrequently noted. In such cases the greatest care must be taken not to radiate too long, and the tube should be buried in the body of the tumor so as to get the full effect of all the rays in all directions. Merely laying the tube in the bladder over the surface of the growth cannot be expected to do much good. The final results of the application of radium to the bladder and prostate tumors cannot at present be estimated from the clinical side, for the reason that the number of cases thus reported is small, and of these many have not been studied microscopically and therefore must be excluded, and most of the reports have been made before a sufficient time has elapsed to make it possible to judge whether the cure is permanent. Certainly, with our knowledge of the slowness of the growth of certain prostatic tumors, some of which do not recur extensively in less than one or two years, it is the height of folly to report a cure at the end of two months. We must rather wait patiently for at least three years before even considering that the results may be permanent."

"It is wiser then not to consider radium as the primary therapeutic choice in the treatment of vesical tumors where operation is possible. If the operation has necessarily incomplete, it may be wiser to radiumize the field thoroughly with large quantities of radium in order to destroy cancer-cells which may have been distributed throughout the field of operation and those which have remained beyond it. When a tumor has recurred after operation the use of large quantities of radium may check the course of the growth for a certain length of time, but the use of small quantities is to be deprecated, for stimulation with increased rapidity of the growth of the tumor may result from the application of insufficient quantity."

"My experience with the use of radium has been limited to a number of cases of extensive vesical carcinoma, and personal observation of the work of Dr. Francis Carter Wood, Director of the Crocker Cancer Laboratories of Columbia University, in experimenting with radium in mice tumors."

"The vesical carcinomata cases were those who had previously been subjected to operation for the removal of the growth. In each instance, the incompleteness of the surgical removal was recognized at the time of operation and the patient at once given the benefit of the application of radium to the unremoved tumor. The technique was the same in each case: Eighty to 100 mg. of radium element with 1 mm. lead, 2 mm. paper, and a thin sheet of rubber were applied to the tumor through a large suprapubic tube. This was left in situ for varying periods of time; the shortest period being six hours, the longest period being thirty-six hours. The number of applications was usually three. The immediate results were similar in all cases; a checking of hemorrhage, an inhibition of bacteriouria with markedly diminished pus in the urine, and, strange as it may seem, a feeling of well-being expressed by the individual. In all the patients, the suprapubic wounds healed quickly.

Each patient died of an extension of the growth within six months of the operation. In no case was there a return of vesical haematuria, the extension being into the pelvis or peritoneal cavity. The number of cases treated was four."

"Appreciating that these cases are not at all conclusive and that they add but little to the scientific data concerning the therapeutic value of radium, it may be of interest to include in these remarks some of the data derived from animal experimentation carried out by Dr. Wood."

"The experiments comprise quantitative studies of the lethal effect of radium on tumor-cells. They are undertaken because of the paucity of information attainable from the writings of various experimenters, working both with human and with animal tumors, on the quantities of radium used, the screens employed, and the time of exposures. These factors being the only ones which would furnish a scientific basis for computing the efficacy of radio-active substances, experiments were carried out with the idea of solving some of the above-mentioned problems."

"Rat and mouse tumors of various types were used. These were treated in vitro and in vivo. Following an exposure of the beta and gamma rays in different amounts and for varying periods of time, portions of the treated tumors and untreated controls were inoculated into animals of the same strain. The alpha rays were not employed, as they are soft rays, causing superficial burns."

"The beta rays, composed of soft, medium, and hard rays, were found to be screened as follows: The absorption limit of the soft rays was 0.4 mm. brass. The medium and hard rays would penetrate such a screen for about 0.8 mm. To absorb the medium and hard beta rays 1.2 mm. of brass was required."

"The gamma rays are the most penetrating. They passed through 1.2 mm. brass. Upon striking the metal used to remove the beta rays, the gamma rays produce a soft secondary beta ray of very slight penetration. These are blocked by a screen of filter paper 5 mm.. in thickness."

"Filtering out the beta rays greatly increased the time required to produce a lethal effect. After a long series of experiments it was found that exposures of seven hours to 100 mg. of radium were necessary to kill the tumor-cells with the beta rays filtered out."

"From a series of inoculation experiments on a previously radiated tumor, it was shown that from as large a quantity of radium as 83 mg. of the element with an exposure of two hours the tissue was not affected at a distance of 1 cm., the inoculated-radiated tumor growing as rapidly as the unradiated controls."

"Wood calls attention to the action being governed by the law of inverse squares. 'If the distance of the tube from the proximal portion of the tumor is 2 mm., and from the distal portion 12 mm., then the effect is not as 1 to 6 but as 4 to 144 or as 1 to 36.' His experiments seemed to prove that in radiated tumors the slowness of growth after inoculation was probably due to injury of the mechanism of mitotic division of the cells. Wood's conclusions are:

1. "Three factors only are dominant in the action of radium on tumors; *i.e.*, the time of exposure, the amount of radium element, and the distance between the tube and the tissue to be acted upon."

2. "The removal by suitable filters of the greater part of the beta rays diminishes proportionally the lethal effect of the radium, but that

the gamma ray effect follows the same law as that governing the beta rays."

3. "Sublethal lethal exposures slow the growth of tumor-cells for some time, while a still shorter treatment seems to stimulate the cellular growth activities."

"Therefore, in the light of our present knowledge, we believe that cures in bladder tumors by the use of radium may be hoped for only in benign papillomata; that it may be possible in certain instances to render the symptoms of vesical malignancy less distressing by intra-urethral and rectal or cross-fire intra-urethral and rectal radiations; that by the time vesical carcinoma has been made clinically manifest the growth has already extended too far to be readily influenced by the amounts of radium at present at our command; that the question of the best management of a case of vesical carcinoma is no different than the management of carcinoma anywhere else in the body—and such is, if the growth is anatomically accessible, wide surgical extirpation followed by every means known of science to treat any unremoved growth or recurrence."

"We may find, however, as further experience develops more ingenious means to use radium intravesically, that radiating the tumor before operation may lessen the danger of tumor transplants occuring at the time of operation."

B. A. Thomas, A.M., M.D., F.A.C.S., Philadelphia. Technique of Operative Treatment of Bladder Tumors. loc. cit. pp. 135-150. "The treatment of bladder tumors may be considered under two chief forms: non-incisional and incisional."

"Non-incisional forms of treatment. Under this heading may be enumerated: (1) high-frequency electro-coagulation, (2) radium, (3) perurethral excision, snare strangulation and cauterization, and (4) irrigations with coagulable solutions."

"Technique of the application of radium. Thus far the sphere of the utility of radium in the treatment of bladder tumors has been largely and should be restricted to inoperable malignant growths, and as a post-operative prophylactic against recurrence. There is no evidence to warrant its substitution for established and well-recognized methods of treatment for operable benign or malignant neoplasmata. Paschkis and Tittinger in 1910 treated successfully a case of sarcoma of the prostate, and the former, the following year, reported on a number of cases of carcinoma of the bladder and prostate, also one of papillioma. The results were poor, due probably to the employment of insufficient radium."

"Through the courtesy of Drs. Charles H. Frazier and Henry K. Pancoast of the University Hospital, I have utilized radium in two cases to supplement surgical procedures. In each case, approximately 110 mg. of radium sulphate or 50.5 mg. of the element radium were employed. Preferably, in extensive inoperable tumors it is best applied through a suprapubic vesical opening, enbedding the capsule in the pathological tissue at various sites for the sake of cross-fire. The capsule, enclosed or not in a rubber tube or catheter, is allowed to remain in one position for two to twenty-four or more hours. The radiations may also be applied to bladder lesions through the urethra. This may be effected with a cystoscope carrying the element as was done by Paschkis, or especially in cases of involvement of the neck by the careful manipulation of a carrier* after previous determination by

cystoscopy of the exact location of the growth. Possibly in the future, with the employment of enormous dosage, taking care to cut off all but the gamma and deep-penetrating rays, the duration of treatment may be shortened and its effectiveness greatly increased. It will be remembered, however, that radium cannot supersede surgery."

Louis E. Schmidt, M.D., F.A.C.S., Chicago. Surgery of the Urinary Bladder. loc. cit. pp. 155-168. "In taking up the palliative operations, how is it possible to select the cases correctly? I need not state that it frequently becomes necessary to do so for other than surgical reasons. This matter cannot be discussed. If an individual shows signs of cachexia or if metastatic conditions are present, or if loss of blood from ulceration of the bladder tumor, or again if pain is excessive as when the internal orifice is involved, it is justifiable to perform the suprapubic operation in the ordinary fashion and remove with curette and scissors or otherwise, and cauterize with thermocautery, 'spark' with the high-frequency current, or 'bake' with diathermy, the parts involved. It is needless to state that these cases demand the establishment of a permanent outlet for the flow of urine. This treatment may be carried out from time to time as found necessary. It also demands the wearing of a urinal. Naturally the question of X-ray therapy and radium or mesothorium treatment is of special interest at this point. However, the question will arise, why use this mode of treatment in these advanced cases only? I believe that this can be readily answered at the present time. Neither the modern X-ray treatment for deep-seated growths nor the application of radium for growths involving the bladder, have as yet been sufficiently tried out to prove them of sufficient value to replace other surgical procedures. However, it must be understood that either or both, if carried out according to the precepts already known, may be used to advantage. I certainly do not believe it wise to rely entirely on one or both, but I have knowledge of one case which has been, to all cystoscopic and other evidence, freed from malignant growth. I must insist in the present stage of our knowledge, that it certainly is advisable, I might even state correct, to treat all cases before and after operation, and all cases not operated upon, with the X-ray. I do not feel quite certain as to radium and mesothorium therapy. It remains to be proved whether it is good practice in cases which have been operated upon and apparently not freed from the growth."

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Harmon Smith, M. D. Papilloma of the Larynx. Discussing the radium treatment of this condition Dr. Smith said: "Radium has been applied in a number of instances, and in some cases marvelous results have been obtained. Abbé reports a case in which the application of 100 mg. of radium kept in position for one-half hour resulted in the rapid disappearance of the growth. Similar experiences have been related by Harris and Culbert. In my experience, however, there is one case presenting sufficient interest to warrant a detailed account, not yielding to radium."

"Case 1. A. V., aged 15, had from birth a husky voice, leading to the supposition that there were congential growths in the larynx. When

*The graduated shaft is a woven-shotted bougie and therefore flexible. Its tip is fitted with a silver capsule, one millimetter in thickness. Surrounding this is a lead cover, one and a half millimeters thick, provided with an oval fenestrum permitting the passage of the effective radium rays. After cystoscopy, by careful manipulation, it is possible to bring the diseased area in close opposition with the fenestrum and conduct cross-fire irradiations.

about 5 years of age he was operated on by Dr. Culbert for multiple laryngeal papilloma associated with the characteristic symptoms. Laryngo-fissure was performed at that time and the entire contents of the larynx cleaned out and the mucosa was cauterized. Within two weeks there was noticeable improvement, which improvement lasted for about six years. At the end of that time there began a recurrence of the symptoms such as hoarseness, dyspnea and imperfect voice production. As this continued to increase he came to my clinic at the Manhattan Eye, Ear and Throat Hospital, Sept. 19, 1911, at which time there could be seen a number of warts on both sides of the larynx, both anteriorly and posteriorly. The voice was very imperfect and of a hoarse, whispering character. The evidence of the former laryngofissure was observable and the movement of the larynx was somewhat imperfect. A tracheotomy was performed and the tube worn for the space of nearly a year. The growths were removed under cocain anesthesia by the direct method, it being reasonable to suppose that surgical removal at this stage, when the patient was approaching puberty, might result in a permanent eradication. They recurred with regular frequency. It was later determined, April 23, 1912, that fulguration should be tried without surgical interference. The growths disappeared following the fulguration and the necessity for another seance did not occur for a period of three months, when they were again removed in the same manner. They occured again at the end of two months, when the third application was made. This time they recurred at the end of a month. After each fulguration, however, a less number of growths returned and the right side of the larynx cleared up almost entirely. The persistent fibrosis together with a large sessile papilloma remained on the left vocal cord and ventrical band. The obstruction to laryngeal respiration, however, was so slight that the trachetomy-tube was removed in October, 1912, since which time local treatment and rest together with partial removal of the growth, whenever it encroached on the larynx, has followed. This procedure was carried out in the belief that the boy was approaching that physiologic change incident to puberty, which would result in a permanent disappearance."

"Radium Treatment.—As this did not take place it was decided in March to employ radium. Through the kindness of Dr. Wolf Freudenthal a tube of radium was placed in the larynx after cocainization, March 19, 1914, and left in for about three-quarters of an hour. There appeared to be a disappearance of some of the thickening around the growth."

"March 26, it was again applied for a period of about one-half hour, following which there seemed to be a marked reaction. The voice has improved under the application of the radium, but the growth continues to recur. There have been three additional applications of radium, varying from fifteen minutes to three-quarters of an hour, but so far as clinical observation goes there has been no dimunition in the size of the growth. The boy is in good health, speaks with a hoarse voice, and while the radium has apparently had little or no effect on it, my belief still holds that physiologic change will ultimately bring about that which therapeutic measures have failed to accomplish." J. A. M. A., Dec. 19, 1914.

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